



TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission 9

Application Number	09/806,370
Filing Date	10/3/2001
First Named Inventor	Holmes
Art Unit	1645
Examiner Name	V. Portner
Attorney Docket Number	33,383-00

ENCLOSURES (Check all that apply)

- | | | |
|---|--|---|
| <input type="checkbox"/> Fee Transmittal Form
<input type="checkbox"/> Fee Attached
<input type="checkbox"/> Amendment/Reply
<input type="checkbox"/> After Final
<input type="checkbox"/> Affidavits/declaration(s)
<input type="checkbox"/> Extension of Time Request
<input type="checkbox"/> Express Abandonment Request
<input type="checkbox"/> Information Disclosure Statement
<input type="checkbox"/> Certified Copy of Priority Document(s)
<input type="checkbox"/> Reply to Missing Parts/Incomplete Application
<input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s)
<input type="checkbox"/> Licensing-related Papers
<input type="checkbox"/> Petition
<input type="checkbox"/> Petition to Convert to a Provisional Application
<input type="checkbox"/> Power of Attorney, Revocation
<input type="checkbox"/> Change of Correspondence Address
<input type="checkbox"/> Terminal Disclaimer
<input type="checkbox"/> Request for Refund
<input type="checkbox"/> CD, Number of CD(s) _____
<input type="checkbox"/> Landscape Table on CD | <input type="checkbox"/> After Allowance Communication to TC
<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input checked="" type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Status Letter
<input type="checkbox"/> Other Enclosure(s) (please identify below): |
|---|--|---|

Remarks

Express Mail No. EO 931 719 794 US
 Customer No. 38199

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Howson & Howson LLP		
Signature	<i>Mary E. Bak</i>		
Printed name	Mary E. Bak		
Date	March 16, 2007	Reg. No.	31,215

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name		Date	

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



33,383-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln. No. : 09/806,370 Confirmation No.: 8568
Appellant : Holmes et al.
Filed : October 3, 2001
TC/A.U. : 1645
Examiner : V. Portner
Docket No. : 33,383-00
Customer No. : 38199
Title : MUTANT CHOLERA HOLOTOXIN AS AN ADJUVANT

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22323-1450

REPLY BRIEF

Sir:

This Reply Brief is timely filed in response to the Examiner's Answer mailed January 17, 2007.

No fee is believed due in connection with this paper. However, the Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Express Mail No. EO 931 719 794 US

I. Status of claims

The pending claims are 1-11, 13-17, 28-37, and 39-44. Claims 1-2 and 13 remain rejected following the Examiner's Answer. Claims 3, 43 and 44 are allowed. Claims 4-11, 14-17, 28-37 and 39-42 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1-2 and 13 are now the subject of this appeal.

II. Summary of claimed subject matter

Appellants' invention as presented in claim 1 is drawn to an antigenic composition that includes at least one antigen from a pathogenic organism selected from among a bacterium, a virus, a fungus and a parasite (page 9, lines 20-25 and original claim 1). The composition also includes an effective adjuvanting amount of a mutant cholera holotoxin (page 9, line 25-26 and original claim 1). The mutant holotoxin has reduced toxicity compared to a wild-type cholera holotoxin (page 9, lines 26-27 and original claim 1) and has an amino acid (other than aspartic acid (Asp)) which replaces the deleted glutamic acid (Glu) which naturally occurs at position 29 of the mature A subunit of the wild-type cholera holotoxin (page 9, lines 28-30 and original claim 1). The mutant holotoxin enhances the immune response in a vertebrate host to the antigen (page 9, lines 20-22).

III. Grounds of rejection to be reviewed on appeal

The issue remaining on appeal is the following:

whether the examiner's rejection of claims 1, 2, and 13 under the provision of 35 USC § 102(b) over Glineur et al., Infection and Immunity, 62(10):4176, 1994 (hereinafter Glineur) should be reversed.

IV. Argument

Claims 1-2 and 13 are rejected under 35 USC § 102(b) over Glineur et al., Infection and Immunity, 62(10):4176 (1994, hereinafter “Glineur”).

The Examiner asserts that Glineur discloses

“a composition comprising a mutant holotoxin with reduced toxicity (see Table 1, page 4181) cholera in combination with additional antigens, specifically a 27 and 12 kDA antigen (see page 4180, column 1, Figure 4, page 4181, lane labeled “E29Δ”), all of the antigens produced by the recombinant host cell *Vibrio cholerae* 569-B-NT upon expression, as well as the expressed ampicillin resistance antigen (see Figure 3, “amp”, “CTA”, “CTB” and page 4180, column 2, paragraph 1), wherein the mutant cholera holotoxin was mutated through deleting the native Glu at position 29, and replacing the deleted Glutamic acid with an amino acid that is neither glutamic acid or aspartic acid (see Figure 2, frame B, line labeled CTX1 E29Δ), wherein the amino acid that replaced the native position 29 Glutamic acid was tyrosine.” Page 4, para 9 of the Examiner’s Answer.

Appellants respectfully request reconsideration and withdrawal of this rejection in view of the following remarks.

As required by MPEP § 2131, in order for Glineur to be a proper 35 USC § 102(b) reference, Glineur must teach *every element* of the claims. However, Glineur does not teach the claims of this application because Glineur does not teach:

- the mutant cholera holotoxin described in Appellants’ claims;
and
- any antigenic composition in which a mutant cholera holotoxin, and specifically the mutant cholera holotoxin described in Appellants’ claims, is used as an adjuvant for another antigen.

Glineur Does Not Teach the Mutant Cholera Holotoxin Mutant Described in Appellants' Claims

Glineur's teachings related to cholera toxin mutants are limited to two mutant cholera holotoxins: (1) the deletion mutant E29 Δ and (2) the substitution mutant E29D. Clearly, the second mutant is explicitly excluded from Appellants' claims.

Glineur's E29 Δ deletion mutant is **not** the same as the mutant holotoxin component of Appellants' claims to an antigenic composition. In the E29 Δ mutant, the wildtype Glu29 is deleted and no other amino acid is inserted in its place. Rather, the remaining amino acids of the holotoxin are shifted to other positions in the sequence. Glineur does not teach in E29 Δ that the Glu that naturally occurs in wild-type cholera holotoxin at position 29 could be replaced with an amino acid other than Asp or that the same would provide a cholera toxin mutant with the properties necessary (including reduced toxicity) for use as an adjuvant in an antigenic composition. It is only Appellants' disclosure that provides the teaching and support for successful use of an amino acid **substitution *other than Asp*** at wildtype position E29 to create a mutant cholera holotoxin useful as an adjuvant in an antigenic composition.

Glineur in no way teaches the requirements of the mutant cholera holotoxin of the antigenic composition of the pending claims. Glineur necessarily fails to teach a recited element in the claim, namely a naturally occurring Glu at position 29, which is in turn substituted by an amino acid other than Asp. Thus, Glineur does not anticipate the mutant cholera holotoxin which is a component of the claimed antigenic composition of the amended claims.

Glineur Does Not Teach an Antigenic Composition in which a Mutant Cholera Holotoxin is used as an Adjuvant for Another Antigen

Despite the Examiner's characterization of Glineur at page 4179-4181 and Figs. 2-4 of Glineur cited above, Glineur does not teach the antigenic composition of

Appellants in which a mutant cholera holotoxin is used as an adjuvant for another antigen. Specifically Fig. 2 at page 4179 simply shows the constructs of the two E29D and E29Δ mutants. The paragraph starting on col. 2, describes the *V. cholerae* expression system for these mutants. The 27 kDA and 12 kDA “antigens” so characterized by the examiner are simply anti-CTX-reactive polypeptides detected in the purified toxin preparations (page 4179, col. 2, last 4 lines through page 4180, col. 1; also Fig. 4). One polypeptide is considered to be an unnicked form of cholera holotoxin subunit A (CTA) and the other is theorized to be a modified form of cholera holotoxin subunit B (CTA) or a proteolytic fragment of CTA. These polypeptides are **not** recited to be antigens to be adjuvanted by the mutant cholera toxin in question. These polypeptides in combination with the mutant cholera holotoxin E29Δ have absolutely nothing to do with the antigenic composition of Appellants’ claims and are not any anticipation of Appellants’ claims.

Glineur clearly does not teach an antigenic composition which contains a first antigen and a mutant cholera holotoxin (CTX) that has an “adjuvant” effect on the first antigen.

In fact, contrary to the Examiner's argument at page 6, paragraph "3." of the Examiner's Answer, the E29D mutant described in Glineur “...had no significant effect on the ADP-ribosyltransferase activity”¹ and consequently would not be useful as an adjuvant, because it had the enzymatic activity of the wild-type CTX. The E29Δ mutant, which contained a simple deletion of position 29, instead of a substitution, was indicated to diminish the enzymatic activity of the holotoxin. This pair of conclusions would lead one of skill in the art to assume that the replacement of the wildtype Glu 29 with another amino acid, as opposed to its deletion without replacement, would **not** reduce the enzymatic activity of the holotoxin. The fact remains that Glineur does not anticipate the antigenic composition of Appellants’ claims. Even if the Examiner were to raise an argument under 35 USC § 103, these

¹ Page 4181, col. 2 and Table 1 of Glineur

inconsistent "suggestions" of Glineur teach away from Appellants' claims, which is evidence of nonobviousness.

In view of the above remarks, this rejection should be withdrawn.

Reversal of the examiner's rejection of the claims under appeal (claims 1-11 and 13) is respectfully requested.

Respectfully submitted,

HOWSON & HOWSON LLP
Attorneys for Appellants

By: Mary E. Bak
Mary E. Bak
Registration No. 31,215
Suite 210
501 Office Center Drive
Fort Washington, PA 19034
Telephone: 215-540-9200
Telefacsimile: 215-540-5818